Remarks

This REPLY is in response to an Office Action mailed October 9, 2008 and to a telephonic interview to be held January 23, 2009 between the Examiner and the undersigned.

Applicants' Interview Summary:

Applicants' representative and the Examiner discussed the following:

1. Claims as proposed to be amended in light of rejections under 35 U.S.C. §101, including the independent Claims 1 and 3, and claims depending therefrom; and

2. Claims as proposed to be amended Claims in light of rejection under 35 U.S.C. §103 over Downs et al., Barnhill et al., and Hemstreet et al., each described in the Office Action.

Rejections Under 35 U.S.C. §101

During the Interview, the Examiner noted that this rejection was for failure of the claims to recite a "concrete, tangible, and useful result." Applicants' representative indicated proposed amendments to Claims 1 and 3 to explicitly recite the limitation: "display of said combined Class A/Class B output on said output device." The Examiner indicated that this amendment would overcome the rejection under 35 U.S.C. §101. The rejection of Claim 4 was discussed, and the Examiner indicated that this rejection would be overcome by the amendment to Claim 3, from which Claim 4 depends.

Rejections Under 35 U.S.C. §103

Applicants' representative pointed out that the instant claims were directed towards improved medical decision systems and methods for improving the accuracy of a medical decision based upon using more than one class of information. Applicant stated that the art cited against the claims does not provide predictions of medical outcome with increased accuracy as claimed: wherein the "combined Class A/Class B output has greater accuracy than either Class A output or Class B output individually." In contrast, the Applicant noted that in the Office Action, the Examiner characterized the Downs reference as follows: "the number of predictions made for each category is then totaled and the one with the highest score (or the most 'votes') is the final predicted category." [Office Action, page 6, five lines from bottom).

Applicants' representative stated that the Barnhill reference is not enabling in that it provides only a suggested field of study, and does not provide any examples, flow charts, or other depictions of actual ways in which accuracy of a medical decision could be made.

Applicants' representative pointed to FIG. 3a as a graphic illustration of a combined outcome depicted as a Venn diagram. Applicants' representative also discussed FIG. 4 for a depiction of how a combined outcome prediction could have increased accuracy compared to accuracies of each class individually. Applicants' representative noted that the paragraphs of the specification (e.g., page 16 of the specification as filed, lines 8-15, page 13, line 5 to page 14, line 10) provide one example of how a combined outcome could be achieved through use of an "exhaustive search method." Applicants' representative also directed the Examiner's attention to other portions of the specification for other methods, a "statistically based specialization method" and a "multilayer perceptron method."

The Examiner noted that the question of obviousness of the claims over Barhnill, Downs and Hemstreet would be considered upon further review of the proposed amendments and remarks made in a subsequently filed REPLY (i.e., this REPLY).

Remarks in Response to Office Action

Rejections Under 35 U.S.C. §101

Claims 1-6 and 8-17 stand rejected under 35 U.S.C. §101 as unpatentable for failing to provide a "concrete, tangible, and useful result." Office Action page 3.

Applicants have amended Claims 1 and 3 to recite the limitation:

"v. display said combined Class A/Class B output on said output device."

Applicants respectfully submit that this amendment defines a "concrete, tangible, and useful result" and requests the rejection to be withdrawn. Applicants note that the rejection of Claim 4 is overcome being dependent from Claim 3 and thereby incorporating the above limitation.

Rejections Under 35 U.S.C. §103

Claims 1-6 and 8-17 stand rejected under 35 U.S.C. §103 as obvious over Downs et al, in view of Barnhill et al. and Hemstreet et al. Office Action, page 6.

Applicants respectfully submit that the combination of Downs, Barnhill and Hemstreet together do not provide an enabled system or method for making medical decisions wherein "said combined Class A/Class B output has greater accuracy than either Class A output or Class B output individually" as in amended Claims 1 and 3.

Applicants provide herewith a Declaration under 37 C.F.R. 1.132 by Dr. Nikola Kirilov Kasabov in support of the application ("Kasabov Declaration"). A true copy of the Kasabov Declaration is included herewith as Exhibit 1. As explained further below, the Kasabov Declaration provides evidence of: (1) the state

of the art, (2) differences between the prior art and the invention, (3) the level of skill in the art, and expresses the Expert opinion that "[t]he pending claims are not obvious over combinations of Downs, Barnhill and Hemstreet," and "[a] person of ordinary skill at the time the application was filed would not know how to modify either combination of the above references to obtain the claimed subject matter."

State of the Art and Level of Ordinary Skill in the Art

According to the Examiner, the art relevant to the current rejections consists of Downs, Barnhill and Hemstreet.

Downs

The Examiner stated (Office Action, page 6, last full paragraph, five lines from bottom) from Downs: "the number of predictions made for each category is then totaled and the ***one*** with the highest score (or the most 'votes') is the final predicted category." Thus, Applicants submit that Downs does not teach or suggest a "combined Class A/Class B output" having "greater accuracy than either Class A output or Class B output individually." as in Applicants' amended Claims 1 and 3.

Further, the Kasabov Declaration provides additional support: "[d]owns does not relate to our invention of integrated classifiers based on separate gene expression and clinical data or any other two or more separate data sets related to the same problem and its outcome. Downs demonstrates the use of the well-known fuzzy ARTMAP neural network model on a single clinical data set. The use of voting is to avoid one of the problems of the fuzzy ARTMAP, namely the dependence of the evolved structure on the order of the sample (example) presentation. However, this has nothing to do with our claimed methods. More specifically, the extracted rules based on Downs are only propositional and based on binary TURE/FALSE input variables and output categories." Kasabov Declaration, paragraph 10.

Barnhill

The Examiner cited to portions of Barnhill asserted to render Applicants' claims obvious (Office Action, page 8, first paragraph).

Applicants respectfully submit that the portions of Barnhill cited are general descriptions of what might be achievable, but at most represent an invitation to invent, but do not provide any enabled methods or systems for improving the accuracy of a "combined Class A/Class B output" as currently claimed.

Further, the Kasabov Declaration provides additional support: "[b]arnhill is a US patent that presents discussion of general approaches and desired results, but does not provide any descriptions of actual methods

to be used or examples of outcomes achieved using those methods to provide increased accuracy of a combined outcome prediction compared to the accuracy of individual outcomes." Kasabov Declaration, paragraph 11.

Hemstreet

Applicants respectfully submit that Hemstreet does not enable any system or method for providing predicting a medical outcome wherein "the error of Combined Class A/Class B output is minimized and said combined Class A/Class B output has greater accuracy than either Class A output or Class B output individually."

Further, the Kasabov Declaration provides additional support: "[h]emstreet is a US patent that, like Barhnill [sic], does not provide any descriptions of actual methods to be used or examples of outcomes achieved using those methods to provide increased accuracy of a combined outcome prediction compared to the accuracy of individual outcomes." Kasabov Declaration, paragraph 12.

Differences Between the Art and the Invention

Applicants respectfully submit that the combination of Downs, Barnhill and Hemstreet together do not render Applicants' claims obvious. As noted above, none of the cited references discloses, teaches, suggests or otherwise provides sufficient guidance to a person of ordinary skill in the art at the time the application was filed to produce a medical decision system or method that produces a result where "said combined Class A/Class B output has greater accuracy than either Class A output or Class B output individually" as in Applicants' claims.

Further, the Kasabov Declaration provides additional support for this position. "[t]he rules extracted using our claimed methods are fuzzy, both quantitatively and qualitatively, and can take any type of variables, including binary, categorical or continuous. Our methods can thus link the continuous variable of gene expression with clinical variables, unlike the methods of Downs, Barnhill or Hemstreet or the combination of those references together." Kasabov Declaration, paragraph 13.

"Examples of our methods and results obtained are described in the application as filed. For example, Page 16 describes one method, based on exhaustive search in the parameter values space. Results of such a method are depicted in FIG. 4, in which it is apparent that parameters $\beta 1$ and $\beta 2$ represent accuracies of individual class predictors, but if either is considered to be zero (i.e., the system uses only one predictor), the overall accuracy is less than the accuracy of a combined system in which both predictors are used, and the results can be greater than either predictor individually." Kasabov Declaration, paragraph 14.

Further, the application as filed illustrates application of methods of the invention in Lymphoma outcome predictions based on a case study (specification, page 17 et seq.).

"A clinical data classifier built on clinical data only had a predictive accuracy of 73.2%. A gene expression classifier, built separately on gene expression data only, had an accuracy of 78.5%. If both clinical and gene expression data is available for a new patient, the predicted outcome by the gene expression classifier will be considered only if it has a higher accuracy of outcome prediction than the accuracy based on clinical information. Thus, using the prior art methods, the patient prediction accuracy will be 78.5%." Kasabov Declaration, paragraph 16.

"If new data is available in which both gene expression information and clinical information is available, the person of ordinary skill would not be able to use the new data to combine with the two existing classifiers and achieve a higher accuracy than the accuracy of any of the classifiers." Kasabov Declaration, paragraph 17.

"In contrast with the prior art methods, our methods (1) and (3) disclose how to do that through tuning three parameters, $\beta 1$, $\beta 2$ and α using the new data set. Applying our method (1) results on the same Lymphoma data in a combined classifier system with a much higher accuracy of 87.5% ! Method (2) of our invention discloses how two separate classifiers can be used on a single new patient data even if there is no other patient data set based on both clinical and gene expression data." Kasabov Declaration, paragraph 19.

"There are no prior art methods disclosed in Downs, Barnhill or Hemstreet nor their obvious combinations that provide how gene expression and clinical data sets related to the same problem (but not necessarily available as a combined data vector for each person) can be integrated into a combined classifier system that produces a better accuracy than any of the single data sets used. Neither of the combinations of the cited references suggest how gene and clinical variables can be integrated in a fuzzy rule (profile) of similar samples to improve the understanding in the interaction between the gene and the clinical variables." Kasabov Declaration, paragraph 20.

"The differences between the combinations of prior art references (Downs, Barnhill and Hemstreet) and our invention are so large that they have not been overcome until our invention." Kasabov Declaration, paragraph 21

Finally, "[a]s a result of our claimed invention, the person of skill in the art is provided new methods and tools to improve diagnosis and evaluation of patient's condition. This desirable result was not possible prior to our invention." Kasabov Declaration, paragraph 22.

Applicants respectfully submit that on the basis of the application as filed and the Kasabov Declaration, that a person of ordinary skill would not have been able to combine the cited references with pre-

existing knowledge in the field to arrive at the invention as currently claimed.

New Claims

Applicants have added new Claims 18-23. Claims 19-22 are dependent claims, in which the sytems (Claims 18-22) are individually limited to particular processes. Support for these new claims can be found at least in the pending claims.

Claim 23 is a new independent claim drawn to the general inventive concept as in Claims 1-17, but not limited to genetic information or clinical information. Support for this claim can be found at least on page 1 of the application as filed, lines 12-13, page 3, lines 24-23, and page 5, lines 20-23.

Conclusion

Applicants respectfully submit that the amendments to the claims, the remarks herein and the Kasobov Declaration have overcome the rejections to the claims, and believe that all claims in the application are patentable. Applicants therefore respectfully request that this amendment be entered into the application, that the Examiner reconsider the current rejections, find the claims allowable, and issue a Notice of Allowance.

A Petition for Extension of Time of one (1) month and the appropriate fee, and a fee for two additional dependent claims are included with this REPLY.

The Commissioner is authorized to deduct from or refund to Deposit Account No: 50-4089 any fee in connection with this REPLY.

If the Examiner believes that a telephonic interview with the undersigned would be useful in moving this application forward, the undersigned cordially invites such an interview.

Respectfully submitted,

Date: February 2, 2009

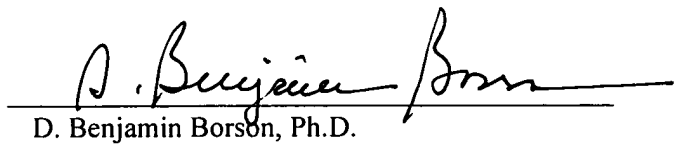
By: 

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Exhibit 1

Declaration Under 37 C.F.R. 1.132

of Nikola Kirilov Kasabov, Ph.D.